INDIAN HEART JOURNAL 65 (2013) 187–190

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Review Article

"On" or "Off" pump coronary artery bypass grafting – Is the last word out?

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A glance at the history of the development of Coronary Artery Bypass Surgery (CABG) throws up the interesting finding that the first milestones were without cardiopulmonary bypass (CPB) support. Off-pump CABG (OPCAB), having predated On-pump surgery, has had a roller coaster ride for want of a clean, still and bloodless field, culminating in the introduction of CABG on CPB (On-pump) by Favaloro in 1967. This development profoundly "democratised" the CABG procedure in that now a broad number of surgeons could achieve better and reproducible results with considerably more optimum operating conditions. The initial enthusiasm for On-pump CABG gradually gave way to concerns regarding its safety, especially with regard to complications arising from CPB, and not CABG per se. Foremost of these relate to microembolic showering during manipulation of the aorta and neurocognitive dysfunction. In addition, CPB triggers a whole-body inflammatory response caused by contact activation of the complement cascade. This leads to multiple organ dysfunction affecting the kidneys, liver, lungs, brain and heart itself.[1] Studies published over a decade and a half ago questioned the safety of On-pump CABG. The proportion of patients recovering without any complication was found to be only 64.3%.[2] In addition, health insurance data and data from clinical studies showed that 10.2% did not leave the hospital within 14 days after the operation and 3.6% of the patients were discharged to a non-acute care facility.[3] These and other observations, pari passu with the development of mechanical and pharmacological organ stabilizers and intracoronary shunts, resurrected OPCAB in the early 1990s.

As regards surgical technique, the actual suture anastomosis of the vessels follows the same technique both in On- and Off-pump surgery. The difference is that unlike On-pump surgery, where the heart is arrested by means of cardioplegia, in Off-pump surgery the area of interest is kept immobile with the help of organ stabilizers while the anastomosis is being performed. Pharmacologic agents like short-acting beta-blockers (e.g. Esmolol) or Adenosine are used in conjunction with these mechanical stabilizers to achieve the goal of a relatively motionless field. Exposure of the heart is aided by retraction devices like the "Starfish", which lift up the apex from the pericardial cavity (Table 1). Retraction can also be achieved by means of folded sponges placed in the pericardial sac to lift the heart, or by pericardial hitching sutures. Distal coronary perfusion is maintained by means of flexible intracoronary shunts introduced into the coronary vessel prior to commencement of the anastomosis (Fig. 1). Although these devices are designed for one-time use, they may be reused after ETO sterilization. This assumes importance as far as cost-containment in a country like India is concerned, giving a further fillip to Off-pump surgery.

Numerous large observational studies and small randomized controlled trials (RCT) have been published in the past 18 years suggesting benefits from OPCAB. Among these are, a reduction in stroke, duration of post-operative ventilation, need for reoperation, bleeding, wound infection, renal failure, post-operative length of stay[4] and decreased atrial fibrillation and inotrope requirement.[5] A major study published in 2001 (the Octopus trial), showing no major differences in cardiac, neurological and neuropsychological outcomes in patients operated On- and Off-pump was also a shot in the arm for Off-pump surgery.[6] However, as with any new technique, initial enthusiasm was somewhat dampened by reports of incomplete revascularization using OPCAB.[7] This and other reports led to the first RCT comparing the two procedures, the Randomized On/Off bypass study (ROOBY) in 2009. At 1-year of follow-up, Off-pump patients had worse composite outcomes

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0019-4832/$ – see front matter
http://dx.doi.org/10.1016/j.ihj.2013.02.008

Table 1 – Commonly used stabilizer/retraction devices.

Name of stabilization device	Stabilization mechanism	Pros	Cons
Medtronic-Utrecht Octopus® tissue stabilization system	Suction	Good stabilization for LAD	Difficulty in LCx territory, cumbersome (discontinued)
Octopus 1	Suction	Good stabilization for LAD	Bulky, cumbersome, difficulty in LCx, long arm causes less stability; (discontinued)
Octopus 2	Suction	Better stabilization, lesser pod height	Stiff pods may cause heart injury (discontinued)
Octopus 3	Suction	Malleable suction pods, better adaptation to heart contour	Increased horizontal motion; (in use)
Octopus 4	Suction	360° arm movement	(in use)
Genzyme Elite stabilizer	Compression of coronary between tapes	No need for shunt	Damage to coronary endothelium, possibility of catching back wall during anastomosis; (not widely used)
Guidant system	Suction	High flexibility of arm	Usable only on custom-made retractor (in use)
Starfish positioning system	Suction	Allows for posterior vessel access	May cause apical ischemia, injury (in use)

of death, myocardial infarction (MI), graft patency and repeat revascularization.[8] The conversion rate from Off- to On-pump procedures was 12.4%, a figure 5 times that reported in the National Database of Thoracic Surgeons! This was bandied as glaring evidence of the participant practitioners' inexperience.[9] The authors had addressed the prickly issue of surgeon experience by doing a sensitivity analysis based on high volume (>50 pre-study cases) versus low volume operators, and had found no significant difference in outcomes. Nonetheless, many have questioned the figure of 50 cases as being insufficient to indicate surgeon experience,[10] whilst disregarding anesthesiologist experience.

As if this was not enough, another nail in the coffin of OPCAB was driven by a recent Cochrane review meta-analysis[11] from Copenhagen considering 10 low-bias trials ($n = 4950$) of a total of 86 RCTs comparing Off-pump with On-pump surgery, which found 30% higher risk of all-cause mortality with Off- vs. On-pump CABG. Other adverse events like MI, stroke, renal insufficiency or repeat revascularization were similar despite a slightly lower number of distal anastomoses Off-pump versus On-pump. In fact the authors, Moller et al hazard to state, "findings suggest that funding sources matter, with the device industry-funded trials less apt to show harm from Off-pump CABG," thereby suggesting that vested interests may be at play. But a major issue with the Cochrane review is that it included just one additional study to the meta-analysis by Afilalo et al (vide infra) which incidentally had showed clear superiority of Off-pump CABG. This additional study, ironically of Moller himself, had a staggering 25% mortality Off-pump, which obviously seriously skewed the results of the review to suggest harm with OPCAB.

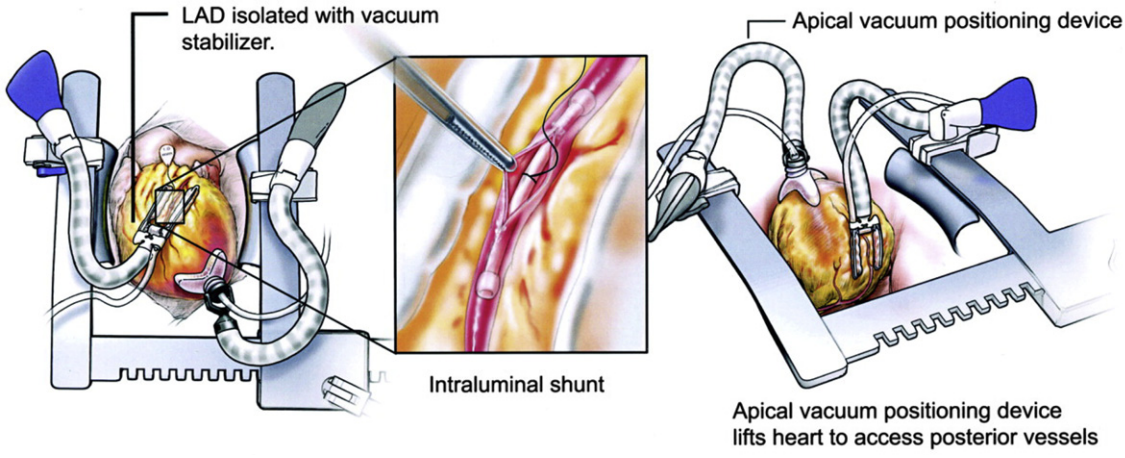

Fig. 1 – Diagrammatic representation of use of stabilizer & retraction/positioning devices and intracoronary shunts in Off-pump surgery. Reprinted from Verma S et al Off pump coronary artery bypass surgery. Fundamentals for the clinical cardiologist. Circulation. 2004;109:1206-1211.

Angelini et al analyzed 2 RCTs comparing Off-pump and On-pump patients 6–8 years following surgery to assess graft patency, major adverse cardiac-related events (MACE), and health-related quality of life. The patient cohort followed up was from the Beating Heart Against Cardioplegic Arrest Studies (BHACAS) 1 and 2 trials.[12] Overall, 10.8% of grafts were occluded across both groups. Further, logistic regression analysis showed no evidence that grafts were more likely to be occluded in OPCAB than in On-pump patients. The differences in MACE-free survival and quality of Life indicators did not approach statistical significance. Although these findings greatly bolstered the case of the proponents of OPCAB surgery, some shortcomings pointed out were that the modality of assessment of graft patency was non-invasive (MDCTA) as against the gold standard of coronary angiography; also, the study was a single center study by a single surgical team, and hence could not necessarily be extrapolated to other surgeons and centers. Another concern with OPCAB is the lesser number of grafts put. But this has long been disproved by a review of 22 RCTs which showed only 0.2 fewer grafts being put in this group compared with On-pump.[13]

A meta-analysis published by Afilalo et al included all published and unpublished RCTs of Off-pump versus On-pump CABG from the MEDLINE, EMBASE and Cochrane databases. It took into consideration a total of 59 trials, encompassing 8961 patients. There was a significant 30% reduction in post-operative strokes with Off-pump surgery [risk ratio (RR) 0.70, 95% CI: 0.49–0.99]. There was no significant difference in mortality (RR: 0.90, 95% CI: 0.63–1.30) or MI (pooled RR: 0.89, 95% CI: 0.69–1.13). In the meta-regression analysis, the effect of OPCAB on all of the clinical outcomes was similar regardless of mean age, proportion of females in the trial, number of grafts per patient, and trial publication date.[13]

The most recent comparison study of the two techniques is the CABG Off or On pump revascularization study (CORONARY Study) published in March this year.[14] The trial randomized 4752 patients undergoing CABG to Off-pump or On-pump groups. There was no significant difference seen in the primary end-points of death, MI, stroke, or new renal failure requiring dialysis at 30 days (Table 2).

There were, however, some differences in secondary outcomes (Table 3), with the Off-pump group showing advantages of less bleeding, respiratory infections, and acute kidney injury, but this group also had fewer grafts performed and had more repeat revascularizations thereby mandating longer term follow-ups before a final verdict.

Table 2 – CORONARY: primary outcomes.

Endpoint	Off-pump (%)	On-pump (%)	HR (95% CI)
Primary composite end point	9.8	10.3	0.95 (0.79–1.14)
Death	2.5	2.5	1.02 (0.71–1.46)
MI	6.7	7.2	0.93 (0.75–1.15)
Stroke	1.0	1.1	0.89 (0.51–1.54)
New renal failure	1.2	1.1	1.04 (0.61–1.76)

Table 3 – CORONARY: secondary outcomes.

End point	Off-pump (%)	On-pump (%)	HR (95% CI)
Repeat revascularization	0.7	0.2	4.01 (1.34–12.0)
Respiratory failure or infection	5.9	7.5	0.79 (0.63–0.98)
Acute kidney injury	28.0	32.1	0.87 (0.80–0.96)
Blood transfusion	50.7	63.3	0.80 (0.75–0.85)
Reoperation for perioperative bleeding	1.4	2.4	0.61 (0.40–0.93)

The investigators thus struck a middle path by recommending either of the two techniques based on patient factors, provided the surgeon was competent in both. For example, if a patient had renal dysfunction or a heavily calcified aorta, OPCAB would be preferred.

Much like the proverbial see-saw, a 1-year follow-up angiographic study of the ROOBY cohort was reported this year by Hattler at the AHA Congress in Orlando. He revealed that Off-pump patients had a lower saphenous vein patency than On-pump, but a similar arterial graft patency rate, leading to less effective revascularization. Grover in an editorial tried to reconcile the difference between the ROOBY and CORONARY trial findings.[15] The latter involved only surgeons experienced in Off-pump surgery, whereas the ROOBY trial also had trainees as operating surgeons. On a conservative note however, he cautioned that any firm conclusions would have to await long term follow-up results.

Training of surgeons in OPCAB techniques has been an issue as it requires a great deal of focus and enthusiasm, apart from safety concerns. However, even this issue has been laid to rest by a recent study from the Bristol Heart Institute[16] that Off-pump surgery is not only safe and reproducible, but the technique can be taught effectively and safely to trainees with clinical outcomes unrelated to either the level of supervision or the seniority of the trainees.

The final frontier for the Off-pump coronary surgeon remains the patient with left main disease as well as those with severely depressed LV function. Here too, lower mortality and complication rates have been demonstrated.[17] OPCAB has been validated with results quite similar to the CORONARY trial in left main stem disease also. Murzi et al showed that OPCAB was associated with lower in-hospital mortality (0.5% vs. 2.9%; $p = 0.001$) and morbidity in terms of stroke, renal dysfunction and pulmonary complications/infections.[18] But the biggest bugbear of OPCAB, viz. fewer grafts (2.7 ± 0.7 vs. 3 ± 0.7; $p = 0.001$) and lower rate of complete revascularization (88.3% vs. 92%; $p = 0.04$) continue to remain. On multivariate analysis, CPB was confirmed to be an independent predictor of in-hospital mortality (OR 5.74; $p = 0.001$). The countervailing pros and cons negating each other lead to similar survivals at 1.5 and 10 years, a fact validated by Cheng et al.[19] OPCAB has also been shown to give superior results in patients with chronic kidney disease.[20]

The International Society for Minimally Invasive Cardiothoracic Surgery (ISMICS) recommendations state that the use of Off-pump bypass reduces perioperative morbidity, neurocognitive dysfunction and hospital length of stay and should be considered especially in high-risk patients, for example,

those with severe ascending aortic calcification, liver disease, renal insufficiency or other systemic processes that may be exacerbated by CPB, in order to reduce morbidity and mortality.[21]

A balanced approach has been advocated by the American Heart Association in their 2011 Guidelines.[22] Based on available data, the guidelines contend, both approaches are reasonable, with certain factors tilting the balance one way or the other. For example, the oft-quoted instance of a patient with a heavily diseased aorta being more amenable to Off-pump surgery. The European Guidelines (2010) on the other hand make no mention of Off-pump surgery, stating instead that over 70% of bypass surgeries worldwide are conducted On-pump[23] (perhaps a diplomatic way of making an undiplomatic point!).

As for our experience at the National Heart Institute in Delhi of over 5000 cases done Off-pump with a conversion rate of less than 1% and mortality of 1.6%, we can safely state that this is an effective technique, provided it is adopted and practiced in spirit as well as letter. The surgeon, and perforce the team, should be well conversant with the nuances of Off-pump techniques, besides being motivated, focused and inclined, and not be a proponent just to join the bandwagon and be counted, whilst jeopardizing the patient's interest. In the end, a doctor's reputation lives through his/her patients, and this is no truer than for a cardiac surgeon. The best technique is that which works best for that particular patient, in the context of his clinical setting and his treating surgeon's repertoire lending credence to our strong belief that it is the surgeon and not the technique, which is at the heart of the problem.

REFERENCES

1. De Jaegere PP, Suyker WJL. Off pump coronary artery bypass surgery. *Heart*. 2002;88(3):313–318.
2. Duhaylongsod F. Minimally invasive cardiac surgery defined. *Arch Surg*. 2000;135:296–301.
3. Roach G, Kanchuger M, Mangano C, et al. Adverse cerebral outcomes after coronary bypass surgery. *N Engl J Med*. 1996;335:1857–1863.
4. Cleveland Jr JC, Shroyer AL, Chen AY, et al. Off-pump coronary artery bypass grafting decreases risk-adjusted mortality and morbidity. *Ann Thorac Surg*. 2001;72:1282–1288.
5. Angelini GD, Taylor FC, Reeves BC, et al. Early and midterm outcome after off-pump and on-pump surgery in Beating Heart against Cardioplegic Arrest Studies (BHACAS 1 and 2): a pooled analysis of two randomised controlled trials. *Lancet*. 2002;359:1194–1199.
6. Van Dijk D, Nierich AP, Eefting FD, et al. The Octopus Study: rationale and design of two randomized trials on medical effectiveness, safety, and cost-effectiveness of bypass surgery on the beating heart. *Control Clin Trials*. 2000;21(6):595–609.
7. Hannan EL, Wu C, Smith CR, et al. Off-pump versus on-pump coronary artery bypass graft surgery: differences in short-term outcomes and in long-term mortality and need for subsequent revascularization. *Circulation*. 2007;116:1145–1152.
8. Shroyer AL, Grover FL, Hattler B, et al, for the Veterans Affairs Randomized On/Off Bypass (ROOBY) Study Group. On-pump versus off-pump coronary artery bypass surgery. *N Engl J Med*. 2009;361:1827–1837.
9. Puskas JD, Mack MJ, Smith CR. On-pump versus off-pump CABG. *N Engl J Med*. 2010;362:851–854.
10. Kieser TM. On-pump versus off-pump CABG. *N Engl J Med*. 2010;362:852–854.
11. Møller CH, Penninga L, Wetterslev J, et al. Off-pump versus on-pump coronary artery bypass grafting for ischaemic heart disease. *Cochrane Database Syst Rev* 2012;(3):CD007224.
12. Angelini GD, Culliford L, Smith DK, et al. Effects of on- and off-pump coronary artery surgery on graft patency, survival, and health-related quality of life: long-term follow-up of 2 randomized controlled trials. *J Thorac Cardiovasc Surg*. 2009;137(2):295–303.
13. Afilalo A, Rasti M, Ohayon SM, et al. Off-pump vs. on-pump coronary artery bypass surgery: an updated meta-analysis and meta-regression of randomized trials. *Eur Heart J*. 2012;33(10):1257–1267.
14. Lamy A, Devereaux PJ, Prabhakaran D, et al. Off-pump or on-pump coronary- artery bypass grafting at 30 days. *N Engl J Med*. 2012;366:1489–1497.
15. Grover FL. Current status of off-pump coronary-artery bypass [Editorial]. *N Engl J Med*. March 26, 2012;366. Published in NEJM.org.
16. Murzi M, Caputo M, Aresu G, et al. Training residents in off-pump coronary artery bypass surgery: a 14 year experience. *J Thorac Cardiovasc Surg*. 2012;143(6):1247–1253.
17. Caputti GM, Palma JH, Gaia DF, et al. Off-pump coronary artery bypass surgery in selected patients is superior to the conventional approach for patients with severely depressed left ventricular function. *Clinics (Sao Paulo)*. 2011 December;66(12):2049–2053.
18. Murzi M, Caputo M, Aresu G, et al. On-pump and off-pump coronary artery bypass grafting in patients with left main stem disease: a propensity score analysis. *J Thorac Cardiovasc Surg*. 2012;143(6):1382–1388.
19. Cheng DC, Bainbridge D, Martin JE, et al, Evidence Based Perioperative Clinical Outcomes Research Group. Does off-pump coronary artery bypass reduce mortality, morbidity, and resource utilization when compared with conventional coronary artery bypass? A meta-analysis of randomized trials. *Anesthesiology*. 2005;102:188–203.
20. Schroeder ME, Chawla L, Zhao Y, et al. Effect of off-pump versus on-pump coronary artery bypass grafting in patients with chronic kidney disease. *Crit Care*. 2012;16(suppl 1):347.
21. Puskas J, Cheng D, Knight J, et al. Off-pump versus conventional coronary artery bypass grafting: a meta-analysis and consensus statement from the 2004 ISMICS consensus conference. *Innovations*. 2005;1(1):3–27.
22. ACCF/AHA Practice Guidelines. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery. *Circulation*. 2011;124:e659.
23. The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Guidelines on myocardial revascularization. *Eur Heart J*. 2010;31:2501–2555.